

REMARKS

In the present communication, claims 1, 3-10, 12-14, 16-18 and 39 have been amended; no claims have been added; and no claims have been canceled. The amendments do not add new matter and are fully supported throughout the specification and claims as filed as discussed below. Accordingly, upon entry of the present amendment claims 1, 3-10, 12-14, 16-18 and 39 will be pending and at issue.

Amendments to the Claims

Various amendments have been made to the claims as provided herein. The amendments are fully supported throughout the specification and claims as filed and do not add new matter. Support for the amendments are provided below as identified in the application as published in U.S. Patent Application Publication 2006/0151900.

Claim 1 has been amended to specify that the substance is provided in a pressure chamber having an inlet and an outlet, wherein the outlet is above the inlet. Support for the amendment may be found throughout the specification, for example, in paragraphs [0036] and [0042]. Claim 1 has been further amended to specify that the molten substance and the liquefied gas or dense gas are allowed to equilibrate to form a homogeneous solution. Support for the amendment may be found throughout the specification, for example, in paragraph [0043]. Claim 1 has been further amended to specify that the carrier fluid passes the solution from the pressure chamber into a vessel of lower pressure to form particles. Support for the amendment may be found throughout the specification, for example, in paragraph [0043].

Claim 18 has been amended to specify that encapsulated particles contain a mixture or combination of the substance and a polymer. Support for the amendment may be found throughout the specification, for example, in paragraph [0023].

Claims 3-10, 12-14, 16-17 and 39 have been amended to clarify claim language, the amendments being supported by the claims as filed.

Restriction Requirement

The Office Action indicates that a further election is required between the alleged different inventions of Group IA (claims 1, 3-10, 12-14, 16-18, and 39) drawn to a method of making a pharmaceutical product; and Group IB (claims 27-29) drawn to a method of treatment. Pursuant to a telephone conversation with Ms. Lisa Haile on December 1, 2008, Applicants confirm election of the invention of Group IA (claims 1, 3-10, 12-14, 16-18, and 39) drawn to a method of making a pharmaceutical product.

Objection to the Drawings

The Office Action alleges Figure 1 must be designated by a legend indicating that Figure 1 represents the prior art because that which is old is illustrated. Without acquiescing to the reasoning presented in the Office Action, and to expedite prosecution of the instant application, Applicants submit a Replacement Sheet herewith including Figure 1, in which Figure 1 is indicated as "Prior Art" as requested. Applicants respectfully submit that no new matter has been introduced into the Replacement Sheet and respectfully request entry of revised Figure 1 and withdrawal of the objection.

Objection to the Specification

The Office Action alleges the specification fails to provide proper antecedent basis for the subject matter of claim 18. Without acquiescing to the reasoning presented in the Office Action, and to expedite prosecution of the instant application, claim 18 has been amended to recite "wherein the encapsulated particles contain a mixture or combination of the substance and a polymer." Accordingly, Applicants respectfully request withdrawal of the objection.

Rejections under 35 U.S.C. §112, Second Paragraph

Applicants respectfully traverse the rejection of claims 18 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Specifically, the Office Action alleges recital of “the polymer” in claim 18 is indefinite since neither claims 1 nor 14 recite “a polymer”. Without acquiescing to the reasoning presented in the Office Action, and to expedite prosecution of the instant application, claim 18 has been amended to recite “wherein the encapsulated particles contain a mixture or combination of the substance and a polymer.” Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. §103

Applicants respectfully traverse the rejection of claims 1, 3-6, 8-12 and 39 under 35 U.S.C. §103(a) as allegedly being obvious over Kerč et al. (*International Journal of Pharmaceuticals*, 182: 33-39 (1999)) in view of Kropf et al. (U.S. Patent No. 6,316,030).

The recent U.S. Supreme Court decision in *KSR International v. Teleflex Inc.* (82 USPQ2d 1385), modified the standard for establishing a *prima facie* case of obviousness. Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

The Office Action alleges that Kerč et al. disclose the method as claimed, with the exception that the reference fails to state that the substance (*e.g.*, drug) is solid before it meets the liquefied gas or that the liquefied gas melts the substance. The Office Action further alleges that the deficient disclosure of Kerč et al. is remedied by the disclosure of Kropf et al. and that it would have been obvious for one of skill in the art to use liquefied gas to melt a solid drug in the method of Kerč et al., either by combining the disclosure of Kropf et al. with the step of Kerč et

al. as they are explicitly disclosed, or by substituting the steps of Kropf et al. with a pre-melting step.

Without acquiescing to the reasoning presented in the Office Action, and in order to expedite the instant application, Applicants have amended claim 1 to further clarify the distinguishing features of the present invention over the prior art. Claim 1 has been amended to specify that the substance is provided in a pressure chamber having an inlet and an outlet, wherein the outlet is above the inlet. Claim 1 has been further amended to specify that the molten substance and the liquefied gas or dense gas are allowed to equilibrate to form a homogeneous solution. Claim 1 has been further amended to specify that the carrier fluid passes the solution from the pressure chamber into a vessel of lower pressure to form particles. As amended claim 1 recites as follows.

A method for manipulating or formulating a solid substance which melts under pressure of a gas without degrading at a temperature which is lower than the melting point of the substance at atmospheric pressure comprising:
providing the substance in a pressure chamber having an inlet and an outlet, wherein the outlet is above the inlet;
applying to the substance a liquefied gas or dense gas to melt the substance without degrading the substance;
equilibrating the molten substance and the liquefied gas or dense gas to form a homogeneous solution; and
contacting the solution with a carrier fluid, wherein the carrier fluid is at substantially the same pressure as the liquefied gas or dense gas, to pass the solution from the pressure chamber through the outlet into a vessel of lower pressure than the pressure of the liquefied gas or dense gas and carrier fluid to form particles of the substance.

Applicants submit that the present invention is directed to a process termed 'Particles from Dense Gas Induced Molten Solutions' (PDGIMS), which is distinguishable over the process known as 'Particles from Gas Saturated Solutions' (PGSS) as disclosed in the cited references. Unlike the PGSS process disclosed in the cited references, in the method of the amended claims (*e.g.*, the PDGIMS process), the molten homogeneous solution formed by a substance being melted by a dense or liquefied gas, is contacted with a carrier fluid which may

also be a dense or liquefied gas and introduced to the pressure chamber through the inlet and positioned below the outlet and at the bottom of the pressure chamber containing the homogeneous solution including the molten substance. The carrier fluid is passed through the molten homogeneous solution and exits the chamber at a higher point through an outlet, having taken at least a part of the molten homogeneous solution with it.

For example, Example 2 of the instant specification (paragraphs [0076]-[0079]) discloses such a process. The Example exemplifies that a critical difference between the configuration of the apparatus used in the claimed method and that of the PGSS process is that the carrier fluid, is passed from the bottom of the pressure chamber to the top through the molten homogeneous solution, such that the carrier fluid containing at least part of the molten homogeneous solution is sprayed through the outlet. Such a configuration prevents saturation of the carrier fluid with the molten homogeneous solution, which advantageously is less viscous than the material sprayed in accordance with the PGSS system (see paragraphs [0049] and [0050] of the specification) preventing blockage of the outlet nozzle and allowing the method to be used with more viscous substances than the PGSS technique.

Applicants respectfully submit that the Office Action fails to establish a *prima facie* case of obviousness with regard to the claims as amended because there would be no motivation to modify or combine the cited references to arrive at the invention as claimed. Kerč et al. disclose a traditional PGSS process and is silent with regard to providing a pressure chamber having an inlet and an outlet, wherein the outlet is above the inlet such that the carrier fluid may be passed through the molten homogeneous solution as claimed. Further, as noted in the Office Action, the reference is silent as to applying a liquefied gas or dense gas to melt the substance in the pressure chamber. Likewise, Kropf et al. fail to disclose such processes as claimed and therefore fail to remedy the deficient disclosure of Kerč et al. Applicants respectfully submit that one of skill in the art would not be motivated to combine the references to arrive at the claimed method in which a pressure chamber having an inlet and an outlet configured above the inlet is utilized to overcome identified problems with the method disclosed in the prior art, such as blocking of the

outlet nozzle and limited applicability of the prior art method to a wider variety of drug substances. Accordingly, the method of the claims as amended is not rendered obvious by the disclosures of the cited references.

Further, the Office Action fails to establish a *prima facie* case of obviousness because, even if one were to combine the teachings of Kerč et al. and Kropf et al., the references fail to teach or suggest each and every limitation of the claimed invention. As discussed above, neither Kerč et al. nor Kropf et al. disclose a method utilizing a pressure chamber having an inlet and an outlet, wherein the outlet is above the inlet such that the carrier fluid may be passed through the molten homogeneous solution as claimed.

Accordingly, for the foregoing reasons, Applicants respectfully request the rejection be withdrawn.

Applicants respectfully traverse the rejection of claims 7, 14 and 16-18 under 35 U.S.C. §103(a) as allegedly being obvious over Kerč et al. (*International Journal of Pharmaceuticals*, 182: 33-39 (1999)) in view of Kropf et al. (U.S. Patent No. 6,316,030), and further in view of Zhu et al. (U.S. Patent Application Publication 2002/0110526).

Applicants respectfully submit that the Office Action fails to establish a *prima facie* case of obviousness with regard to the claims as amended because there would be no motivation to modify or combine the cited references to arrive at the invention as claimed. As discussed above, both Kerč et al. and Kropf et al. fail to disclose a method utilizing a pressure chamber having an inlet and an outlet, wherein the outlet is above the inlet such that the carrier fluid may be passed through the molten homogeneous solution as claimed. Similarly, Zhu et al. also fails to disclose such a method and therefore fails to remedy the deficient disclosures of both Kerč et al. and Kropf et al. Applicants respectfully submit that one of skill in the art would not be motivated to combine the references to arrive at the claimed method in which a pressure chamber having an inlet and an outlet configured above the inlet is utilized to overcome identified problems with the method disclosed in the prior art, such as blocking of the outlet nozzle and

limited applicability of the prior art method to a wider variety of drug substances. Accordingly, the method of the claims as amended is not rendered obvious by the disclosures of the cited references.

Accordingly, for the foregoing reasons, Applicants respectfully request the rejection be withdrawn.

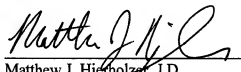
Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

The Commissioner is hereby authorized to charge the total amount of \$65.00 to cover the payment of a One-Month Extension of Time fee (\$65.00) to Deposit Account No. 07-1896. No other fees are deemed necessary with the filing of this paper. However, the Commissioner is further authorized to charge any additional fees, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,

Date: April 8, 2009



Matthew J. Hienholzer, J.D.
Registration No.: 53,021
Telephone: (858) 638-6638
Facsimile: (858) 677-1465

DLA Piper LLP (US)
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO Customer No.: 28213